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LETTER TO THE EDITOR

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Development of pancytopenia in a patient with COVID-19

To the Editor,

The coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Laboratory findings of COVID-19 include lymphopenia and elevated inflammatory markers. However, pancytopenia is less common. Here, we reported a case of an elderly patient who developed pancytopenia with COVID-19.

A 69-year-old male presented to the emergency room in February 2020 with fever, dry cough, fatigue, and dyspnea for 15 days. The patient has a history of right lung adenocarcinoma status post chemoradiation but has been in remission for 2 years. Of note, the patient's wife was recently diagnosed with COVID-19. At the time of presentation, a complete blood count panel showed white blood cell count (WBC) of 3.32×10^9/L, hemoglobin of 87 g/L, and platelet of 206×10^9/L, which were close to his baseline. Chest computed tomography without contrast showed ground-glass opacities of the right lower lobe. An oropharyngeal (OP) swab was performed and tested positive for SARS-CoV-2. The patient was admitted to the general medical floor and started on moxifloxacin and umifenovir. One day later, the patient was transferred to the intensive care unit due to increased oxygen requirement. Repeat laboratory work showed WBC 2.16×10^9/L with neutrophil 0.39×10^9/L and lymphocytes 0.78×10^9/L, hemoglobin 62 g/L with a mean corpuscular volume of 117, and platelet 37×10^9/L. C-reaction protein was 33.5 mg/L; D-dimer was 14.02 mg/L; ferritin was 1500 ug/L; lactate dehydrogenase was 353 IU/L; interlukin-6 (IL-6) was 15.9 pg/mL. Bilirubin, uric acid, folate, and vitamin B12 were within a normal range. Fecal occult blood was tested negative. Peripheral smear showed no schistocytes. During the hospital course, the patient's blood counts continued dropping. IL-6 peaked at 45.0 pg/ml on Day 19. On Day 23, the patient developed neutropenia with neutrophil 0.33×10^9/L; filgrastim was given. On Day 25, hemoglobin was 49 g/L with reticulocytes of 3.94%; two units of packed red blood cells were transfused. Bone marrow was examined to determine the cause of pancytopenia. Core biopsy showed bone marrow cellularity of 45% with normal trilineage hematopoiesis. (Figure 1) Bone marrow differential showed depressed proliferation of myeloid cells with myeloid:erythroid ratio (M:E ratio) of 0.7; megakaryocytes were present and other cell differentials were normal. Flow cytometry showed no clonal expansion. The patient's clinical condition improved with supportive care. On Day 24, a repeat OP swab was tested negative for SARS-CoV-2. The patient was discharged home on Day 45, with WBC 1.16×10^9/L, neutrophil 0.56×10^9/L, hemoglobin 56 g/L, and platelet 389×10^9/L.

Lymphopenia is found in a majority of patients with COVID-19 and its severity has been shown to be associated with clinical outcomes.[1] Platelet and hemoglobin levels are usually normal, although patients with severe disease could have thrombocytopenia.[2] This patient initially presented with low normal WBC and platelets, along with moderate macrocytic anemia. During hospitalization, the patient developed pancytopenia requiring filgrastim and transfusion. Upon discharge, although platelet counts have recovered, the patient still had leukopenia and anemia. No bleeding source or nutrient deficiency was identified; no concurrent viral infection was identified. Moreover, moxifloxacin is rarely associated with pancytopenia and no case of umifenovir-associated pancytopenia was reported, making medication-induced pancytopenia less likely. The decreased M:E ratio in our patient indicates bone marrow suppression was the cause of pancytopenia. Bone marrow suppression can be seen in various viral infections, including EBV, HIV, CMV, and Parvovirus B19.[3] After viral infection, an antigenic epitope on myelocytes could be exposed, leading to the production of autoantibody and destruction of blood cells. The angiotensin-converting enzyme 2 receptor, target of the SARS-CoV-2, has been identified in bone marrow albeit at a low level.[4] Therefore, it is possible that direct infection of myelocytes could lead to bone marrow suppression. Another key feature of COVID-19 is an elevated level of proinflammatory cytokines. It is well known that certain cytokines, such as the interferons and tumor-necrosis factor-α, can affect hematopoietic stem cells and

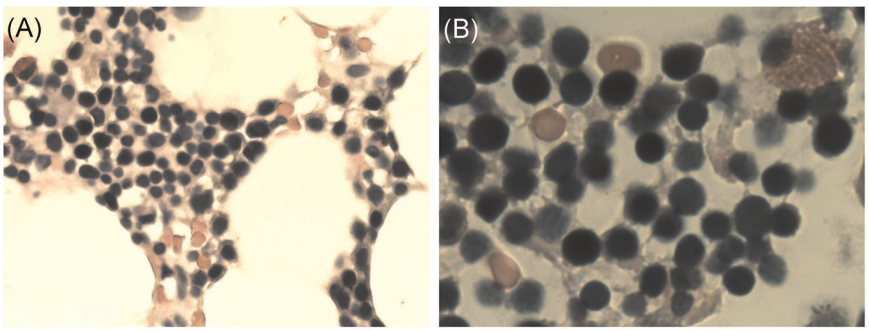

FIGURE 1 Bone marrow biopsy of a patient with coronavirus disease 2019 developing pancytopenia. Normocellular bone marrow (45%), with a normal number of megakaryocytes, increased erythropoiesis, and normal maturation of the granulopoiesis. Bony trabeculae appear normal with no osteosclerosis. (A) ×400, (B) ×1000 magnification

impair hematopoiesis.[5] Moreover, given the history of chemoradiation, this patient might have baseline bone marrow dysfunction, contributing to pancytopenia. In addition, the lung has been recently identified as a site for platelet biogenesis and a reservoir for hematopoietic progenitors.[6] With SARS-CoV-2 infection and lung injury, it is possible that the destruction of lung hematopoietic progenitors could also contribute to the pancytopenia.

In summary, we reported a case of pancytopenia associated with COVID-19 likely caused by bone marrow suppression.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Written consent for publication was obtained from the patient. Yi Zhao, Jingsong He, and Jiasheng Wang wrote the manuscript. Wei-Ming Li, Mi Xu, Xu Yu, Wei Wu, Chunyin Sun, Zherong Xu, and Weifang Zhang were involved in patient care. Yu Hu and He Huang supervised and revised the manuscript.

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